DRIVE
Development of Robust and Innovative Vaccine Effectiveness

innovative medicines initiative

D6.2 Report with the definition of the ethics policies handbooks collection

DRIVE 116134-2
DEVELOPMENT OF ROBUST AND INNOVATIVE VACCINE EFFECTIVENESS

[WP6 – Project management, coordination and sustainability]

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Summary

In all the studies carried out by the DRIVE consortium, high standards of research ethics will be upheld. Additionally, participants to any DRIVE activities are expected to ensure that any relevant national and regional laws, policies and guidelines will be adequately followed.

In order to estimate influenza vaccine effectiveness, DRIVE will collect data from different study sites. No clinical studies will be performed directly by the DRIVE consortium, and no direct contact will occur between the DRIVE consortium and the study subjects. However, DRIVE may use data collected in clinical studies and/or clinical trials conducted by the partner organisations of DRIVE. An Ethics Advisory Board (EAB) will provide oversight for ethics related aspects of DRIVE. Work Package 8 of DRIVE will ensure that certain specific ethics requirements are met.

All research activities in DRIVE will be organised in accordance with the Charter of Fundamental Rights of the EU, the Declaration of Helsinki, the Convention of Council of Europe on Human Rights and Biomedicine, the Ethical Rules of the Seventh Framework Programme, and, where applicable, the Opinions of European Group on Ethics in science and new technologies, Good Epidemiological Practice, Guidelines for Good Pharmacology Practices and the standards of the International Conference on Harmonisation on Good Clinical Practice.

This document summarizes the ethics practices of DRIVE and catalogues other relevant international, national and regional laws, policies and guidelines to be followed, such as those considering ethics requirements, informed consent, vulnerable groups, physical interventions, handling of samples, data collection, secondary use of previously collected data, data processing, data management and data interpretation.

1. Methods

A review of international rules and guidelines concerning DRIVE was made. Current data-providing partners of DRIVE were asked to provide references to the relevant legislation and other policies and guidelines in their countries. This document will be updated as needed, e.g. when new Associate Partners join DRIVE.

2. Research ethics in DRIVE

2.1 Ethics principles of DRIVE

In all the studies carried out by the DRIVE consortium, high standards of ethical practice will be upheld. Participants to any DRIVE activities are expected to ensure that any relevant national and regional laws, policies and guidelines will be adequately followed.

All activities will follow the ethical principles of respect, beneficence, non-maleficence and to contributing to society's knowledge and practice. All activities will be carried out in the spirit of scientific integrity, excellence, cooperation, honesty, accountability and transparency.

2.2 Ethical implications of DRIVE activities

DRIVE will collect data from different study sites. No clinical studies will be performed directly by the DRIVE consortium, and no direct contact will occur between the DRIVE consortium and the study subjects. However,

DRIVE may use data collected in clinical studies and/or clinical trials conducted by the partner organisations of DRIVE.

The research under DRIVE will not involve human embryonic stem cells, human embryos, foetal tissues/cells, processing of human genetic information or animal studies. No harm to the environment is expected, nor is there any conceivable potential for military use or malevolent misuse of the study results.

DRIVE may analyse data resulting from the participation of vulnerable populations, such as children or pregnant women, or adults unable to consent, provided that all applicable laws, policies and guidelines have been followed in collecting the data.

In some instances, respiratory samples (e.g. nasal/oral/nasopharyngeal swabs or lavages) collected by study sites could be sent to laboratories of DRIVE partners for further analysis. This transfer will be performed according to the national regulations and with a courier with experience in handling biological samples. Only a virological analysis will be performed in these laboratories, with no test that would allow human genomic analysis. This situation would be immediately notified to IMI and copies of the transfer agreements between the sites and the laboratories will be obtained and submitted to IMI in the next yearly deliverable covering ethics requirements. A copy of these will also be kept in DRIVE file.

2.3 Data management & protection

All data received by DRIVE will be either previously anonymized or codified by the institution that collects that, or aggregated. In any case, DRIVE will only receive a local ID that will not permit DRIVE to identify the subject and no personally identifiable information (PPI) will be accessible to DRIVE. Data linkages will be undertaken by authorised staff such as those authorised by the relevant national authorisation bodies. Data will be linked by a unique patient identifier and supplemented, if necessary, by checks using gender, date of birth, area of residence and treatment centre.

The transfer of the data will depend of the local legislation. Countries like Finland, Italy or Spain may share individual anonymized or pseudonymized data to be used in pooled analyses. In countries where this is not possible, aggregated data may be shared. Authorizations from the relevant competent data protection bodies or clearance from the dedicated data protection officer of the corresponding institution will be obtained and recorded on DRIVE register and incorporated in Deliverable 8.2 “POPD - Requirement No. 3” and updated in the yearly ethics requirements updates as part of the annual report. In any case, DRIVE will always comply with the EU General Data Protection Regulation and with the local laws, and authorizations for data transfer will be obtained, if needed, by the local bodies or institutions in charge of data protection.

DRIVE’s practices concerning data management and data protection will be detailed in a separate Data Management Plan (deliverable 4.2).

2.4 Ethics approvals

In many countries, influenza vaccine effectiveness is part of ongoing program evaluations required by the ministries of health. As these evaluations are a requisite part of the public health institutions’ work and considered as part of routine evaluation, they usually fall outside the mandate for Ethics Committees. In these cases, no formal approval from Ethics Committees will be required.

Other centres not included in the above definition that collect data and share it with DRIVE will ensure that the Ethics Committee of the institution has approved the study, including the collection of data from vulnerable populations. The approvals/authorisations will be obtained individually by each participating centre, which will keep its own copy for record. Copies of all ethics approvals will be submitted to IMI prior to the start of the annual studies, and filed by DRIVE.

2.5 Ethics advisory board

The Ethics Advisory Board (EAB) will provide oversight for all ethics related aspects for studies conducted in the context of DRIVE. The EAB will be responsible for reviewing the proper application of the ethical rules and providing advice to the DRIVE partners, the General Assembly and the Steering Committee on the compliance of any European relevant ethical applicable laws, regulations and guidelines.

As per the DRIVE Consortium Agreement, the Ethics Advisory Board will be composed of three experts with detailed knowledge of ethical policies at European level. Nominations for membership of the EAB may be submitted to the Steering Committee, which shall ensure that the composition of the EAB is appropriate to provide the guidance required. The members of the EAB shall have no recent affiliation to any consortium members; however, they may hold other independent external advisory functions inside DRIVE (e.g. as members of the Quality Control & Audit Committee).

The Ethics Advisory Board will advise the General Assembly and the Steering Committee upon request of the Project Leader together with the Coordinator and provide non-binding advice to the General Assembly and the Steering Committee as decision making support. The EAB will meet upon request of the General Assembly or Steering Committee but at least once a year.

2.6 Work Package 8

Work Package 8 (Ethics requirements) sets out the ethics requirements that the project must comply with. WP8 is headed by FISABIO and SP and will produce four deliverables, each answering a specific requirement:

- **Information on human samples** (*The applicants must provide detailed information on the human samples to be used by the project. The applicants must also report on the collection and analysis of samples by third parties if the sample collection and/or analysis is informed by or steered by the project. If applicable, relevant approvals / authorisations and transfer agreements must be obtained and copies of these must be submitted to the IMI prior to the start of relevant research activities*.)

- **Data sources** (*The applicants must provide, update and maintain an internal register with data sources and must demonstrate for each data source that the primary or secondary use within the project is lawful. Depending on the legal framework in the relevant jurisdictions, the applicants must obtain authorisations/approvals/clearances/notifications from the relevant competent data protection bodies or clearance from the dedicated data protection officer of the institution in charge of the data processing / transfer.*)

- **Approvals, authorisations & clearances** (*When applicable, ethical approval/authorisation by the competent national/regional Data Protection Authority or clearance from the dedicated Data Protection Officer of the institution for the intended data collection, processing and transfer must be provided to the IMI before the commencement of the related project activities. When relevant, the authorisations must provide evidence that the intended data transfer between partners and third parties, and the crossborder transfer from Non-EU countries are in compliance with national and EU legal framework*.)

- **Anonymization and rights of data subjects** (*In case data that are to be anonymised (and not de-identified /coded/pseudonymised) the applicants must provide details on the protocols and how the applicants ensure that data cannot be re-identified with reasonable efforts. In case data are processed in a person-identifiable manner, the applicants must provide details how data subjects will be informed or must justify, in line with Directive 95/46/EC and the upcoming EU General Data Protection Regulation, why data subjects are not informed about the use of data. If applicable, the applicants must also outline how the project will ensure the rights of data subjects and how these rights of data subjects will be organisationally managed*.)

3. International rules and guidelines concerning DRIVE

Whenever applicable, research activities in DRIVE will be organised in accordance with

- The Charter of Fundamental Rights of the EU, available at http://ec.europa.eu/justice/fundamental-rights/charter/index_en.htm
- The Declaration of Helsinki, available at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
- The Convention of Council of Europe on Human Rights and Biomedicine, available at https://rm.coe.int/168007cf98 and the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, available at https://rm.coe.int/168008371a
- The Ethical Rules of the Seventh Framework Programme
- The Opinions of EGE (European Group on Ethics in science and new technologies), available at https://ec.europa.eu/research/ege/index.cfm
- The European Union Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data, available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31995L0046:EN:HTML
- The upcoming EU General Data Protection Regulation, available at http://data.consilium.europa.eu/doc/document/ST-5419-2016-REV-1/en/pdf
- Good Epidemiological Practice (GEP) by International Epidemiological Association, accessible at http://ieaweb.org/good-epidemiological-practice-gep/
- Guidelines for Good Pharmacology Practices (GPP) by International Society for Pharmacoepidemiology, available at https://www.pharmacoepi.org/resources/guidelines_08027.cfm
- The standards of the International Conference on Harmonisation on Good Clinical Practice, available at https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf
- European Code of Conduct for Research Integrity, available at http://ec.europa.eu/research/participants/data/ref/h2020/other/hi/h2020-ethics_code-of-conduct_en.pdf
- Directive 2006/24/EC of 15 March 2006 on the retention of data generated or processed in connection with the provision of publicly available electronic communication services or of public communications networks
- Directive 2002/58/EC of the European Parliament and of the Council of 12 July 2002 concerning the processing of personal data and the protection of privacy in the electronic communications sector (Directive on privacy and electronic communications)
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF
- Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the

requirements for authorisation of the manufacturing or importation of such products, available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:091:0013:0019:en:PDF

- The upcoming Regulation (EU) no 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, available at https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

4. Finland: applicable laws and policies

Partner: THL

Background

In Finland, types of studies whose results may be considered for sharing with DRIVE include pure register-based studies, clinical observational studies, clinical interventional studies or a mixture of these.

Acts and decrees

Ministry of Social Affairs and Health, Finland. Act on the Status and Rights of Patients. 1992/785 (with 19 amendments)

- Partly available as unofficial translation at: http://www.finlex.fi/fi/laki/kaannokset/1992/en19920785.pdf
- Contains legislation on patients' rights, including the confidentiality of information in medical records.

Ministry of Social Affairs and Health, Finland. Personal Data Act. 1999/523 (with 7 amendments)

- Partly available as unofficial translation at: http://www.finlex.fi/fi/laki/kaannokset/1999/en19990523.pdf
- This will change in 25.5.2018, when the EU Regulation no. 2016/679 will be directly applicable in all EU member states and probably at the same time a new national complementary law will enter into force
- Contains guidance on the use of personal data, including subjects participating in medical research.

Ministry of Social Affairs and Health, Finland. Medical Research Act. 1999/488 (amended by 2004/295, 2010/794 and 2015/143)

- Partly available as unofficial translation at: http://www.finlex.fi/fi/laki/kaannokset/1999/en19990488.pdf
- Based on
    - The Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States and relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
    - The Commission Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products

- This will in the next years be replaced by 'Regulation (EU) 2014/536 of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC' and national complementary laws on medical research and clinical trials

Ministry of Justice, Finland. Act on the Openness of Government Activities 1999/621 (with 26 amendments)

- Partly available as unofficial translation at: https://www.finlex.fi/fi/laki/kaannokset/1999/en19990621.pdf

Statistics Act 2004/280 (with 4 amendments)

- Contains the terms under which data can be delivered from official statistics
- No translation available

Laki terveydenhuollon valtakunnallisista henkilörekistereistä 1989/556 (amended by 1991/115 and 1993/38)

- Contains additional information on the terms under which data can be delivered from official statistics
- No translation available

Communicable Diseases Act 2016/1227

- Contains the basis for maintaining the Infectious Disease Register and delivering data from it
- No translation available

Act on the National Institute for Health and Welfare 2008/668 (amended by 2009/1067, 2010/1231 and 2015/751)

- Partly available as unofficial translation at: https://www.finlex.fi/fi/laki/kaannokset/2008/en20080668.pdf
- Regulates the function of THL as a statistical authority as referred to in the Statistics Act, to maintain data files and registers relevant to the field as separately provided by law and to take care of the knowledge base of its field of activity and the utilisation of that knowledge base;

Patient Injury Act 1986/585 (with 23 amendments)

- No translation available

Archives Act 1994/831 (Arkistolaki) (with 10 amendments)

- Contains regulation on archives of public institutions including THL
- No translation available

Information Society Code 917/2014

- Partly available as unofficial translation at: https://www.finlex.fi/fi/laki/kaannokset/2014/en20140917.pdf
- Aims to ensure the confidentiality of electronic communication and the protection of privacy.

Act on the Medical Use of Human Organs and Tissues (101/2001)In addition, several decrees further regulate the details of the implementation of the respective acts

Binding regulations

Finnish Medicines Agency FIMEA, Finland. Administrative regulation 32/03.01.01/2012

- Contains the procedure for notification to the Competent Authority concerning clinical trials and interventional studies concerning medicinal products
- NOTE: in Finland, studies are interpreted as interventional if the article 2.c of the Directive 2001/20/EC does not apply, i.e. even if the intervention is not medication but e.g. a diagnostic test, with some case-by-case consideration.
- Partly available as unofficial translation at: http://www.fimea.fi/documents/542809/842303/25594_Maarays_2_2012_Clinical_trials_on_medicinal_products.pdf

Approvals and opinions

Register-based studies

If only register-based data is used in the study, the approval has to be available from the data controller of the respective register. Thus, THL issues the approvals to use the health registers managed by THL (e.g. Care Register for Health Care, Register of Primary Health Care visits, Vaccination register, National Infectious Diseases Register, Medical Birth Register, please see https://www.thl.fi/en/web/thlfi-en/statistics/information-on-statistics). Before issuing the approval, THL also requires a favourable opinion of the Institutional review board (IRB) of National Institute for Health and Welfare.

Other registers used for research of vaccine effects comprise

- Social Insurance Institution of Finland (KELA): Benefits register, Prescription centre and Prescription archive
- Population register: population data, coverage of other register data
- Statistics Finland: Causes of death register

In addition to approvals, the sampling of data has to be separately applied for, and the data sampling may take considerable time. If data is collected from registers without consent of the study participants, or the data will be transferred outside EU/EEA, the data collection has to be notified to the Office of the Data Protection Ombudsman.

Clinical studies

A favourable opinion is needed from one regional ethics committee (the area of action of principal investigator or the area where the study mainly will be performed). Of interventional studies, a notification has to first be sent to the National Committee on Medical Research Ethics (TUKIJA), which may refer the evaluation to the regional ethics committee.

Interventional studies and trials have also be notified to the Finnish Medicines Agency FIMEA, which is the national authority tor supervising these studies.

Institutional approvals must be available from institutes where the participants are recruited and from the institutes whose personnel take part of the conduction the trial.

Informed consent procedure in clinical studies

The process for obtaining informed consent is described in the Medical Research Act 6 § (amendment 23.4.2004/295), 6a§ (amendment 20.2.2015/143), 7§ and 8§.

In addition, according to the Degree 2016/65, 3§, the informed content document must include:

1) the research subject's name, personal identity code or date of birth, and address

2) that the information referred to in 6 § (3) has been given to the research subject and data about the giver of the information

3) which other sources information concerning the research subject will be gathered from

4) whom the information gathered in the context of the research can be delivered to and how the confidentiality of the information is protected

5) the research subject's voluntary consent

6) a mention of the right to withdraw the consent without it affecting the research subject's right to receive the care he or she is in need of

7) a mention of that the data collected up to the time of withdrawing the consent will be managed according to the 6 a § of the Medical Research Act.

5. Italy: applicable laws and policies

Partner: ISS

Background

The study is conducted within the context of the existing National sentinel influenza surveillance system (InfluNet) implemented in the 1999/2000 season that has been set up under the agreement signed by the State-Regions Conference on 28 September 2000 (Acts No. 1031).

InfluNet is regulated every season by a Ministry of Health Note on the Surveillance and Prevention of seasonal influenza in Italy (available at: http://www.trovanorme.salute.gov.it/norme/renderNormsanPdf;jsessionid=JCEbZYZ6VGHBhyATrnouzg__.sgc4-prd-sal?anno=2017&codLeg=60180&parte=1%20&serie=null) that is distributed to all Italian regions, and is based on voluntary participation of an average of 1,046 (range: 955-1,305) general practitioners (GPs) and pediatricians (Ps) per season, covering about 2% the general population by region and age group. Within the InfluNet system, the test-negative case-control study has been established in order to produce IVE estimates in preventing primary care consultation due to laboratory-confirmed influenza infection.

Acts and decrees

National data protection law (Legislative Decree no. 196 of 30 June 2003)

- As expressed in the law, the data protection of sensitive data is the "Processing of sensitive data by public bodies shall only be allowed where it is expressly authorised by a law specifying the categories of data that may be processed and the categories of operation that may be performed as well as the substantial public interest pursued." No sensitive data are collected with the InfluNet system and the

GPs and pediatricians and Local Health Authorities have the rights to access to sensitive health data of recruited cases.

- Available at http://www.garanteprivacy.it/web/guest/home/docweb/-/docweb-display/docweb/1311248

Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016

- On the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)
- Available at: http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A32016R0679

Other guidelines

Code of conduct and professional practice applying to the processing of personal data for statistical and scientific purposes

- Available at: http://www.garanteprivacy.it/web/guest/home/docweb/-/docweb-display/docweb/1115480

Authorisation no. 9/2014

Authorisation no. 2/2014

General Authorization to Process Personal Data for Scientific Research

Concerning Processing of Data Suitable for Disclosing Health or Sex Life

Additional documents on the DPA website may be relevant, such as those governing processing of sensitive data by associations and foundations (for example, Authorisation no. 3/2014 and Authorisation for data transfers in compliance with standard contractual clauses, both controller to controller and controller to processor).

Approvals and opinions

Being a surveillance activity and not a clinical trial (no intervention) no research permits or ethics approval are required.

6. Valencia (Spain): applicable laws and policies

Partner: FISABIO

Acts and decrees

Law 14/2007, of biomedical research

- Regulates biomedical research, autonomy of the patient, data collection and biobanking
- Available at https://www.boe.es/buscar/doc.php?id=BOE-A-2007-12945

Royal Decree 1716/2011

- A degree detailing the use of biological samples and biobanks

Organic Law 15/1999, Personal data protection

- Contains requirements for data protection)
- Available at https://www.boe.es/buscar/act.php?id=BOE-A-1999-23750

Law 41/2002, Autonomy of the patient, rights and obligations in relation information and medical documentation

- Regulates the use of medical records for health care and health research
- Available at https://www.boe.es/buscar/act.php?id=BOE-A-2002-22188

Order SAS/3470/2009, Post authorization, observational studies with human medicines

- Legislation of post authorisation studies with human medicines. Includes the requirements and processes)
- Available at https://www.boe.es/buscar/doc.php?id=BOE-A-2009-20817

Royal Decree 577/2013, Pharmacovigilance of human medicines

- Spanish requirements for pharmacovigilance, including effectiveness studies
- Available at: https://www.boe.es/buscar/doc.php?id=BOE-A-2013-8191

Royal Decree 223/2004

- On clinical trials with medicines

Law 29/2006

- On the rational use of medicines and health products

Ministerial Order 256/2007

- On good clinical practice and the requirements to authorize the manufacture or importation of drugs in research for human use.

The following decrees and resolutions of the Regional Government of Valencia on clinical trials and observational studies regarding medicines and health products

- Correction of errors of Decree 73/2009
- Decree 73/2009
- Decree 17/2012
- Resolution of July 16, 2009

Approvals and opinions

The Clinical Research Ethics Committee (El Comité Ético de Investigación Clínica, CEIC) is the independent body of FISABIO responsible for ensuring the protection of the rights, safety and well-being of the participants in a clinical trial through an opinion on the trial protocol, the suitability of the researchers and the adequacy of the facilities, as well as the methods and documents that will be used to inform the subjects of the trial in order to obtain their informed consent.

The Standard Operating Procedures of CEIC are available at http://fisabio.san.gva.es/documents/10157/78724243-c425-464d-ae19-0551d405e66e.